Oxyfunctionalization of Hydrocarbons: 10. Hydroxylation of Benzene and Alkylbenzenes with 30% Hydrogen Peroxide in Pyridinium Polyhydrogen Fluoride

George A. Olah*, Takashi KIYUKI, Alexander P. Fung

Hydrocarbon Research Institute, Department of Chemistry, University of Southern California, University Park, Los Angeles, California 90007, U.S.A.

Acid-catalyzed electrophilic hydroxylation of aromatics has recently received considerable attention, and a number of methods have been developed to bring about such conversions1-2. Liquid hydrogen fluoride has been noted as a catalyst for the hydroxylation of aromatic compounds with aqueous hydrogen peroxide3. Effective electrophilic hydroxylation of aromatics was also carried out with 90% hydrogen peroxide in superacidic media at low temperature4.

A drawback for these processes is that the reaction either has to be carried out at superatmospheric pressure in an autoclave (due to the volatility of HF) or involves 90% hydrogen peroxide as a reagent at low temperatures, which tends to limit its practical application. Aromatic hydrocarbons (toluene and m-xylene) have also been oxygenated by hydrogen peroxide/boron trifluoride etherate reagent to produce phenols and other oxygenated products in low yields5.

In the present investigation, it was found that 30% aqueous hydrogen peroxide is a very effective reagent for the hydroxylation of alkylbenzenes in pyridinium polyhydrogen fluoride solution6, providing a convenient way to carry out the reaction under mild conditions and at atmospheric pressure. Yields obtained and isomer distributions are summarized in the Table.

\[
\text{Ar-H} + \text{H}_2\text{O}_2 \stackrel{\text{HF}, \text{pyridine} \times 30 \% \text{ H}_2\text{O}_2, 0^\circ}{\text{Ar-OH}}
\]

The reaction is assumed to proceed via electrophilic substitution by protonated hydrogen peroxide: \(\text{H}_2\text{O}_2 = \text{HO}^+ \cdot \text{OH}^-\). The reaction of the monoalkylbenzenes shows predominant ortho/para orientation in accordance with typical electrophilic aromatic substitution. Steric factors, as usual, also play an important role in determining isomer distributions in the reactions. For example, the hydroxylation of \(\text{t}-\text{butylbenzene} gave only the para isomer, the ortho position being sterically hindered.}

It is interesting to point out that in several cases the position of the methyl group in the phenolic products differs from that of the starting hydrocarbons. Control experiments showed that pyridinium polyhydrogen fluoride itself caused no rearrangement of alkylbenzenes or their related phenols. Therefore, it is considered that during the hydroxylation reaction, the ease of intramolecular 1,2-methyl shifts in the arenium ion type intermediates is responsible for the obtained rearranged products.

Displacement of the methyl group by ipso hydroxy attack accounts for the formation of \(p\)-cresol (6%) from \(p\)-xylene.

Similarly, the hydroxylation of \(t\)-butylbenzene occurs with some loss of the \(t\)-butyl group. However, since we found that benzene itself is hydroxylated to phenol under the reaction conditions one can not completely rule out the possibility of protolytic cleavage of the \(t\)-butyl group.

Hydroxylation of Aromatic Compounds:

To a vigorously stirred solution of the corresponding arene (0.01 mol) in (HF)/pyridine (70% = 30% w/w) (30 ml), a solution of 30% hydrogen peroxide (0.012 mol) (Mallinckrodt Co.) in (HF)/pyridine (10 ml) is added. After the stirred reaction mixture has been kept at 0° for 3 h, it is quenched with ice-water, extracted with ether, the extract washed with 10% sodium hydrogen carbonate solution to remove acid, and then extracted with 10% sodium hydroxide solution. Any insoluble material is filtered, but no further attempt for its characterization is made. The dried organic layer is distilled and found after removal of solvent to contain only unreacted aromatics (identified by I.R. and G.L.C.). Following acidification of the base extract and ether extraction, the etheral layer is dried and the phenolic products are obtained after removal of solvent by distillation. For analysis aliquots of the products were si-
Table. Hydroxylation of Arenes with 30% with Hydrogen Peroxide in Pyridinium Polyhydrogen Fluoride

<table>
<thead>
<tr>
<th>Arene</th>
<th>Reaction time</th>
<th>Yield (^a) [%]</th>
<th>Isomer distribution [%] (^b)</th>
<th>b.p./torr</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>5 h</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toluene</td>
<td>3 h</td>
<td>47</td>
<td>42 (2)</td>
<td>5 (3)</td>
<td>53 (4)</td>
</tr>
<tr>
<td>Ethylbenzene</td>
<td>3 h</td>
<td>58</td>
<td>51 (2)</td>
<td>5 (3)</td>
<td>44 (4)</td>
</tr>
<tr>
<td>t-Butylbenzene</td>
<td>2.5 h</td>
<td>38</td>
<td>84 (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-Xylene</td>
<td>3 h</td>
<td>53</td>
<td>82 (2.5)</td>
<td>12 (2.4)</td>
<td>p-cresol 6</td>
</tr>
<tr>
<td>o-Xylene</td>
<td>3 h</td>
<td>53</td>
<td>80 (2.3)</td>
<td>16 (3.4)</td>
<td>4 (2.6)</td>
</tr>
<tr>
<td>Mesitylene</td>
<td>3 h</td>
<td>40</td>
<td>100 (2.4, 6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Yield of isolated phenolic products (based on starting arenes).
\(^b\) Based on gas chromatographic analysis of phenolic products. Figures in parentheses show position of substituents.

16% of phenol was also obtained in the reaction.

\(\text{H}_2\text{O}_2\text{.}^{10}\)

lated by \(\text{N,O-bis(trimethylsilyl)trifluoroacetamide (Pierce)}\) and identified as the trimethylsilyl ethers by G.L.C. Gas chromatographic analyses were carried out using a Varian Associates Model 3700 gas chromatograph equipped with 25 ft x 0.25 mm i.d. OV 101 glass capillary column eluted with Helium, or 10 ft x \(\frac{1}{8}\) in OV 101 column, which was also eluted with Helium. Peak areas were measured with a Varian CDS 111 electronic integrator.

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